REMARKS

Applicant has cancelled the nonelected claims 1-27 and 30-38 as required under 37 CFR 1.144. Applicant has amended Claim 28 and added new Claims 39, 40, and 41. Support for these new Claims can be found in the Specification on page 30.

Objection

The Examiner has objected to Claim 28, because the term "prostate-derived" cell is not clear. Claim 28 has been amended to refer to a "prostate cell". Applicant believes this addresses the Examiner's objection .

Final Rejection under 35 U.S.C. §112

In the latest Office Action, the Examiner has basically repeated her contention that because the state of the art in this technical field is so highly unpredictable, the Specification is not enabling for the claimed invention. The Examiner states (page 4) "although there were many examples of immunoconjugates ...being used to selectively kill cells, these examples are not applicable to the claimed invention, because different antibodies behave in vivo differently, and one cannot predict that the PROST 03 immunoconjugate...could be used successfully in vivo for killing prostate cancer cells or for treating prostate cancer".

The Examiner is clearly saying that the Applicant must provide examples of *in vivo* killing of a prostate cell expressing SEQ ID NO: 2 or treating prostate cancer with an immunoconjugate of the invention in order for the Specification to be enabling. The PTO has indicated that *in vivo* data is not necessary to support utility (see *In re Brana*, 51 F .3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995; PTO Revised Interim Utility Guidelines). Applicants believe that it is similarly not necessary to have *in vivo* data to show enablement, and it is clear that concerns raised by the Examiner are ones which would be addressed during the normal preclinical/clinical evaluation of a drug candidate.

Let us review exactly what the Applicants have demonstrated, what would be known by one skilled in the art of immunotherapy, and what a combination of this knowledge would reasonably enable.

First, **PROST 03 is a prostate-specific target.** In the Specification (Example 5, pg 43, and Figure 5), Applicants have demonstrated that PROST 03 is significantly expressed only in prostate tissue (normal and tumor), with over-expression in prostate tumor, and would, therefore, be a good choice for prostate-targeted immunotherapy. The treatment of choice for localized prostate cancer is surgery or radiation. Once prostate cancer has metastasized, which often occurs relatively early in the course of the disease, there are no cures and the treatment of advanced prostate cancer focuses on the elimination of metastatic cells. "To achieve effective anti-metastatic activity against disseminated lesions will require either systemic delivery or localized delivery of an agent .....Therapy with specific antibodies also has great potential and is being used clinically as an adjuvant in several cancers (Timme et al. (2003) *Currrent Drug Targets* 4:251-261, pg 252). Because of the specificity of PROST 03, the likelihood of toxicity to other tissues when using anti-PROST 03 antibodies is extremely low, and targeting to prostate tissue high.

Second, **PROST 03 is a cell-surface protein.** PROST 03 shows strong sequence homology to a family of sugar/proton transporter proteins, which are known to be cell-surface proteins (see Specification, pages 3 and 14). It would be clear to one skilled in the art that a cell-surface protein which shows selective tissue expression is an ideal candidate for targeted immunotherapy.

Third, **Applicant has generated antibodies** to peptides derived from the PROST 03 sequence (see Specification, Example 4) and **has shown that such antibodies stain prostate tumor tissue and prostate metastases** (see Specification, Example 5 and Figure 6). The technology to produce other forms of antibodies (e.g. monoclonal, chimeric, humanized or human), which are known to have characteristics that may be preferred for therapeutic uses (see Specification, pg 16), are well within the knowledge-base of one skilled in the art.

Based on these facts, it is clear that the Applicant has provided enough information regarding the properties of PROST 03 to lead one skilled in the art of immunotherapy to have a reasonable expectation of the successful use of immunoconjugates of PROST 03 to kill prostate cells or as a therapeutic approach for metastatic prostate cancer.

As stated in a recent review: "One approach to antibody therapy is to fuse antibodies to cell surface markers with cytotoxic agents. Several clinical trials are underway using this approach such as radiolabeled antibody, j591, to prostate specific membrane antigen or SGN-15, a doxyrubicin conjugated antibody to Lewis Y antigen that is highly expressed in prostate cancer (Timme et al. (2003) *Current Drug Targets* 4:251-261). The Examiner has not met her burden in providing any information which would make one skilled in the art doubt that PROST 03 might be an equally useful therapeutic target, but has merely brought up various issues that one skilled in the art would always encounter in the normal process of preclinical drug evaluation.

In view of the foregoing, Applicants request that the Examiner reconsider her rejection of the claims under Section 112, first paragraph.

Conclusion:

Applicants respectfully submit that with the submission of the newly amended Claims 28 and 29 and the arguments presented above, the rejection of Claims 28 and 29 should be withdrawn and that the Claims are in condition for allowance.

Respectfully submitted,

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